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| 09/678,016 | 10/02/2000 | Keith P. Wilson | VPI/96-03 DIV2 | 7947 |
| 1473 | 7590 | 05/04/2004 | EXAMINER | |
| FISH & NEAVE 1251 AVENUE OF THE AMERICAS 50TH FLOOR NEW YORK, NY 10020-1105 | | | ALLEN, MARIANNE P | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1631 | |

DATE MAILED: 05/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

8/14

Office Action Summary

Application No.

09/678,016

Applicant(s)

WILSON ET AL.

Examiner

Marianne P. Allen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23,27-52,55 and 58 is/are pending in the application.
- 4a) Of the above claim(s) 41-51 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 23,27-40,52,55 and 58 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☒ Claim(s) 23,27-52,55 and 58 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 2/24/04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/13/04 has been entered.

Claims 1-22, 24-26, 53-54, 56-57 and 59-62 have been cancelled. Claims 23, 27-52, 55, and 58 are pending.

Election/Restrictions

Claims 41-51 remain directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Although claims 41, 44, 47, 50, and 51 have been amended to depend upon elected claims 23, 29, 32, and/or 35, these claims are not directed to methods of selecting chemical entities. The steps added by these claims are directed to different end results, namely designing a compound or complex by assembling two chemical entities. As set forth in the prior Office action, these methods can be shown to be distinct from the method for selecting a chemical entity based on its ability to associate with a binding pocket as each method has different method steps and/or goals and would require a non-coextensive search (patent and non-patent literature).

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution

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on the merits. Accordingly, claims 41-51 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 23, 27-40, 52, 55, and 58 have been examined.

Claim Rejections - 35 USC § 112

Claims 23, 27-40, 52, 55, and 58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 23, 29, 32, and 35 have been amended to be directed to methods for “selecting at least one of a plurality of chemical entities based on its ability to associate” and now require “wherein said docking utilizes energy minimization” and “selecting at least one of said chemical entities based on said quantified association.” No basis has been pointed to for these amendments and none is apparent. Note that while the preamble discusses “at least one of a plurality” the body of these claims does not dock more than one chemical entity. There are no iterative steps and there is no plurality. In addition, the basis for selection following output of the quantified association is unknown.

Claim 35 as amended appears to dock a chemical entity to IMPDH where XMP* and MPA are already docked. No basis is seen for this.

Basis for the amendments to claim 37 are not understood. Applicant points to basis at page 29, lines 7-17; however, the method as now claimed does not appear to be disclosed here.

Claim 39 remains new matter. The specification does not disclose or contemplate producing other crystals giving the same binding pocket coordinates as set forth in claims 23, 29, and/or 32. Note that these claims are directed to any crystal and not the one exemplified that gave the structure coordinates of Figure 1.

Claim 40 indicates that the fitting operation is performed through visual inspection. Basis is stated to be on pages 19 and 29. These portions of the specification indicate that while visual inspection may be the starting point, the process must involve docking chemical entities of interest within the binding pocket using known algorithms. There does not appear to be basis for using visual techniques alone. Applicant's response does not appear to address this rejection.

Claims 55 and 58 are directed to methods where the quantified association is deformation energy. No basis has been pointed to and none is apparent. Note that page 33 discloses designing inhibitors having a particular deformation energy. The claims are not so limited.

Should this new matter rejection be overcome, claims 23, 27-40, 52, 55, and 58 would be subject to the following enablement rejection.

Independent claims 23, 29, 32, and 35 have been amended to be directed to a method for selecting at least one of a plurality of chemical entities based on its ability to associate with all or any part of a binding pocket defined by given structure coordinates. The steps set forth are to dock the chemical entity with all or part of the binding pocket, quantify the association, output the quantified association to a suitable output hardware, and select at least one chemical entity based on the quantified association.

The claims as written do not result in the goal of the preamble. Claims 23, 29, 32, and 35 have been amended to be directed to methods for "selecting at least one of a plurality of chemical entities based on its ability to associate" and now require "wherein said docking utilizes energy minimization" and "selecting at least one of said chemical entities based on said quantified association." Note that while the preamble discusses "at least one of a plurality" the body of these claims does not dock more than one chemical entity.

Applicant was advised in the prior Office action that if the preamble of the claim was amended to be directed to quantifying the association of a chemical entity (or similar language) such a method is considered to lack patentable utility as it produces no information of any value to those of ordinary skill in the art. That is, unless the method discriminates in some fashion between chemical entities that associate and those that do not or between chemical entities that associate better than other chemical entities or that a particular degree of association results in a desired outcome (e.g. inhibition), one of ordinary skill in the art would not know how to use the information produced. This rejection has not been made at this point solely because each of the independent claims requires a "selecting" step.

It is again noted that the specification does not exemplify the method as claimed that is merely quantifying in the absence of specific criteria for selection. Example 6 is prophetic, yet even this example is directed to designing inhibitors which must necessarily associate to the degree necessary to inhibit the biological activity. These prophetic examples indicate the desirability of a lowest-energy bound conformation or molecule strain energy of 10 kcal/mol or less. The entirety of the specification appears to be directed to identifying chemical entities with a particular degree of associating. The claims lack the criteria by which selection is made. As

such, one of ordinary skill in the art does not know how to select the at least one of said chemical entities.

As set forth in the prior Office action, with the exception of claims 55 and 58 (as amended) one of ordinary skill in the art is not guided as to what type of value the claims require (e.g. estimated interaction energy, conformation energy, etc.) for quantification. Even for claims 55 and 58 the value required to guide one of ordinary skill in the art to select the chemical entity is not provided. The specification provides no examples using the structural coordinates of Figure 1 in the methods as claimed. No docking of chemical entities is performed for any chemical entity, no analysis of the results leading to quantification of the association is performed, no output of this quantification is exemplified for the IMPDH binding pocket using any computational means, and no selection by any criteria is performed.

Claims 23, 27-40, 52, 55, and 58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are confusing as they require selecting at least one of a plurality; however, there are no repetitive or iterative steps in the body of the claims.

The claims are confusing as they do not provide any criteria by which a chemical entity is selected.

The claims are unclear as to how a selection is made after all quantified associations are output to suitable output hardware. That is, as the claims are written, any selections are never saved or communicated in any fashion.

Claim 35 is confusing in discussing association with all or part of a molecular complex. It is unclear if the chemical entity is docked to the IMPDH structure where XMP* and MPA are already docked. Dependent claim 36 makes this more confusing in that the complex could be limited to amino acids 1-514 of IMPDH.

Claim 38 is confusing as claims 23, 29, and 32 are not directed to molecular complexes (see step e). Furthermore, the preamble of claim 38 is not consistent with the steps of the claim. The added steps are contacting the chemical entity with the molecule or molecular complex and monitoring the catalytic activity. Monitoring is not consistent with selection. It appears that these steps are directed to wet chemistry; however, the claim does not possess limitations to a physical molecule, molecular complex, or chemical entity. Structure coordinates representing part of a molecule as well as structural coordinates representing a chemical entity are all that is required. Alternatively, if these steps were intended to be computational simulations for catalytic activity this is unclear. Finally, "monitoring" is considered to imply checking or evaluating for a particular level or type of catalytic activity and the claim does not make clear what attribute is of interest.

Claim Rejections - 35 USC § 103

Claims 23, 27-37, 40, 52, 55, and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over N. Claude Cohen et al. (1990).

Cohen et al. teaches computer programs and methods for docking chemical entities to a binding pocket wherein docking utilizes energy minimization, quantifying the association, outputting the results, and selecting chemical entities based on those results. Visual inspection by means of computer graphics can be used. Input for the program is three dimensional structure

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information. Shape complementarity and molecular dynamics are disclosed (see claim 37). The software disclosed would calculate deformation energy (see claims 55 and 58). See abstract and at least pages 891 and 893 describing modeling techniques and available software.

The difference between the prior art and the claimed invention is the recited three dimensional structure information. This information is descriptive information stored on or employed by a machine. This information is fed into a known algorithm whose purpose is to compare or modify those data using a series of processing steps that do not impose a change in the processing steps and are thus nonfunctional descriptive material. The claimed invention uses known software to solve a known problem in a conventional manner. The instant specification acknowledges known prior art computer modeling techniques. Neither the specification nor the claims set forth any special, non-obvious modifications to the known, conventional software and method steps. A method of using a known comparator (e.g. computer modeling techniques known in the prior art to N. Claude Cohen et al.) for its known purpose to compare data sets does not become nonobvious merely because new data becomes available for analysis. Nonfunctional descriptive material cannot render nonobvious an invention that would have otherwise been obvious. See *In re Gulack*, 703 F. 2d 1381, 1385 (Fed. Cir. 1983) and MPEP 2106. Applicant is also directed to the Trilateral Project WM4 Report on Comparative Study on Protein 3-dimensional (3-D) Structure Related Claims at http://www.uspto.gov/web/tws/wm4/wm4_3d_report.htm. See in particular discussion regarding case 7, claim 1.

Conclusion

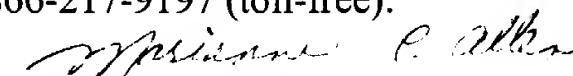
No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 571-272-0712. The examiner can normally be reached on Monday-Thursday, 5:30 am - 1:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571-272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Marianne P. Allen
Primary Examiner
Art Unit 1631
5/3/04

mpa